General

Guideline Title

Varicose veins in the legs. The diagnosis and management of varicose veins.

Bibliographic Source(s)

National Clinical Guideline Centre. Varicose veins in the legs. The diagnosis and management of varicose veins. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. 23 p. (Clinical guideline; no. 168).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Note: The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendations). See the end of the "Major Recommendations" field for further descriptions of the strength of recommendations.

Information for People with Varicose Veins

Give people who present with varicose veins information that includes:

- An explanation of what varicose veins are
- Possible causes of varicose veins
- The likelihood of progression and possible complications, including deep vein thrombosis, skin changes, leg ulcers, bleeding, and thrombophlebitis. Address any misconceptions the person may have about the risks of developing complications.
- Treatment options, including symptom relief, an overview of interventional treatments and the role of compression
- Advice on:
    - Weight loss (for guidance on weight management see Obesity: Guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children [NICE clinical guideline 43])
    - Light to moderate physical activity

- Avoiding factors that are known to make their symptoms worse if possible
- When and where to seek further medical help

When discussing treatment for varicose veins at the vascular service[1] tell the person:

- What treatment options are available
- The expected benefits and risks of each treatment option
- That new varicose veins may develop after treatment
- That they may need more than 1 session of treatment
- That the chance of recurrence after treatment for recurrent varicose veins is higher than for primary varicose veins

Referral to a Vascular Service

Refer people with bleeding varicose veins to a vascular service[1] immediately.

Refer people to a vascular service if they have any of the following.

- Symptomatic[2] primary or symptomatic recurrent varicose veins
- Lower-limb skin changes, such as pigmentation or eczema, thought to be caused by chronic venous insufficiency
- Superficial vein thrombosis (characterised by the appearance of hard, painful veins) and suspected venous incompetence
- A venous leg ulcer (a break in the skin below the knee that has not healed within 2 weeks)
- A healed venous leg ulcer

Assessment and Treatment in a Vascular Service

Assessment

Use duplex ultrasound to confirm the diagnosis of varicose veins and the extent of truncal reflux, and to plan treatment for people with suspected primary or recurrent varicose veins.

Interventional Treatment

For people with confirmed varicose veins and truncal reflux:

- Offer endothermal ablation (see Radiofrequency ablation of varicose veins [NICE interventional procedure guidance 8] and Endovenous laser treatment of the long saphenous vein [NICE interventional procedure guidance 52]).
- If endothermal ablation is unsuitable, offer ultrasound-guided foam sclerotherapy (see Ultrasound-guided foam sclerotherapy for varicose veins [NICE interventional procedure guidance 440]).
- If ultrasound-guided foam sclerotherapy is unsuitable, offer surgery.
  If incompetent varicose tributaries are to be treated, consider treating them at the same time.

If offering compression bandaging or hosiery for use after interventional treatment, do not use for more than 7 days.

Non-interventional Treatment

Do not offer compression hosiery to treat varicose veins unless interventional treatment is unsuitable.

Management During Pregnancy

Give pregnant women presenting with varicose veins information on the effect of pregnancy on varicose veins.

Do not carry out interventional treatment for varicose veins during pregnancy other than in exceptional circumstances.

Consider compression hosiery for symptom relief of leg swelling associated with varicose veins during pregnancy.

Footnotes

[1]A team of healthcare professionals who have the skills to undertake a full clinical and duplex ultrasound assessment and provide a full range of treatment

[2]Veins found in association with troublesome lower limb symptoms (typically pain, aching, discomfort, swelling, heaviness, and itching).

Definitions:

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, "Do not offer…") are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses "consider" when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) pathway titled "Varicose Veins in the Legs Overview" is available from the NICE Web site .

Scope

Disease/Condition(s)

Varicose veins

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Obstetrics and Gynecology

Surgery

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Physician Assistants

Physicians

Guideline Objective(s)

- To offer best practice advice on the care of adults aged 18 years and over with varicose veins in the legs
- To give healthcare professionals guidance on the diagnosis and management of varicose veins in the legs, in order to improve patient care and minimise disparities in care across the UK

Target Population

Adults (18 years and older) with primary or recurrent varicose veins in their legs

Note: This guideline does not apply to the following populations or issues:

Children and young people (younger than 18)
People with venous malformations
People with varicose veins in places other than their legs
Management of leg ulcers (other than the role of ablative truncal venous interventions)
Management of spider veins (thread veins)
Management of pelvic varicose veins not located on the legs

Interventions and Practices Considered

1. Providing information to patients, including:
    - What varicose veins are
    - Possible causes
    - The likelihood of progression and possible complications (e.g., deep vein thrombosis, skin changes, leg ulcers, bleeding and thrombophlebitis)
    - Treatment options
2. Referral to vascular service
3. Duplex ultrasound
4. Endothermal ablation
5. Ultrasound-guided foam sclerotherapy
6. Surgery
7. Compression bandaging or hosiery (only if interventional treatment is unsuitable)

8. Management during pregnancy

Major Outcomes Considered

- Health-related quality of life (for example, Medical Outcomes Study Short From 36, EQ-5D)
- Patient-assessed symptoms
- Physician-reported outcome (venous clinical severity score or venous disability score)
- Complications from varicose veins (skin ulcer occurrence or changes, haemorrhage, and phlebitis)
- Adverse events from intervention (including stroke, deep vein thrombosis, and neuropraxia)
- Recurrent varicose veins
- Vein reflux and occlusion (blockage) rates
- Reflux
- Sensitivity and specificity per tested vein
- Patient satisfaction
- Symptom scales (normally visual analogue scale [VAS])
- Days to return to work/normal activity

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing the Review Questions and Outcomes

For intervention reviews, review questions were developed in a framework encompassing definitions of the population, intervention, comparison, and outcomes (PICO). For prognostic reviews, questions were developed with a framework of population, prognostic factor, and outcomes. For diagnostic reviews, questions were developed with a framework of population, index tests, reference test, and target condition. The scope of these questions was further defined by the 'protocol' for each question, where, alongside the question framework, search and analysis strategies and the inclusion and exclusion criteria were defined (see Appendix C of the full version of the original guideline document). This was to guide the literature-searching process and to facilitate the development of recommendations by the Guideline Development Group (GDG). Review question protocols were drafted by the NCGC technical team and refined and validated by the GDG. The question protocols were based on the key clinical areas identified in the scope (see Appendix A in the full version of the original guideline document). A total of 15 review questions were identified. The finalised review questions are summarised in Table 1 of the full version of the original guideline document.

Groups for Special Consideration

Two groups for special consideration were identified during the scoping stage:

- Pregnant women with varicose veins
- People with recurrent varicose veins

No specific review questions were developed for the populations of pregnant women with varicose veins and people with recurrent varicose veins, as both population groups were included in all the review questions. However because of the importance of these two groups, relevant findings that

had been collected during the course of answering the guideline review questions were collated and discussed by the GDG.

Searching for Evidence

Clinical Literature Search

The aim of the literature search was to systematically identify all published clinical evidence relevant to the review questions. Searches were undertaken according to the parameters stipulated within the NICE Guidelines Manual (2009) (see the "Availability of Companion Documents" field). Databases were searched using medical subject headings and free-text terms. Foreign language studies were not reviewed and, where possible, searches were restricted to articles published in the English language. All searches were conducted in MEDLINE, EMBASE, and the Cochrane Library, and were updated for the final time on 17th October 2012. No papers after this date were considered.

Search strategies were quality assured by cross-checking reference lists of highly relevant papers, analysing search strategies in other systematic reviews, and asking GDG members to highlight any additional studies. The questions, the study types applied, the databases searched, and the years covered can be found in Appendix F in the full version of the original guideline document.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the inclusion criteria.

Health Economic Literature Search

Systematic searches were undertaken to identify relevant health economic evidence within the published literature. The National Health Service Economic Evaluation Database (NHS EED), the Health Economic Evaluations Database (HEED), and Health Technology Assessment (HTA) database were searched using broad population terms and no date restrictions. A search was also run in MEDLINE and EMBASE using a specific economic filter with population terms and limited to the years 2009 onwards. Where possible, searches were restricted to articles published in the English language.

Economics search strategies are included in Appendix F in the full version of the original guideline document. All searches were updated for the final time on 17th October 2012. No papers published after this date were considered.

Evidence of Effectiveness

The research fellows:

- Identified potentially relevant studies for each review question by reviewing titles and abstracts from the relevant search results. The full papers for these potentially relevant studies were then obtained.
- Reviewed the full papers against pre-specified inclusion/exclusion criteria to identify studies that addressed the review question in the appropriate population and reported on outcomes of interest (review protocols are included in Appendix C in the full version of the original guideline document).

Inclusion/Exclusion

See the review protocols in Appendix C in the full version of the original guideline document for full details.

Key population inclusion criteria were adults (18 years or over) with primary or recurrent varicose veins in their legs. Pregnant women were specifically included. Key population exclusion criteria were:

- Children and young people (younger than 18)
- People with venous malformations
- People with varicose veins in places other than their legs

Conference abstracts were not automatically excluded from the review but were initially assessed against the inclusion criteria and then further processed only if no other full publication was available for that review question or there was a scarcity of evidence. In this case the authors of the selected abstracts were contacted for further information.

Evidence of Cost-effectiveness

The health economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts – full papers were then obtained

- Reviewed full papers against pre-specified inclusion/exclusion criteria to identify relevant studies

Inclusion/Exclusion

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost–utility, cost–effectiveness, cost–benefit, and cost–consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially applicable as economic evidence.

Studies that only reported cost per hospital (not per patient), or only reported average cost effectiveness without disaggregated costs and effects, were excluded. Abstracts, posters, reviews, letters/editorials, foreign language publications, and unpublished studies were excluded. Studies judged to have an applicability rating of 'not applicable' were excluded (this included studies that took the perspective of a non-Organisation for Economic Co-operation and Development [OECD] country).

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable UK analysis was available other less relevant studies may not have been included. Where exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist (The Guidelines Manual) and the health economics review protocol in Appendix C in the full version of the original guideline document.

When no relevant economic analysis was found from the economic literature review, relevant UK National Health Service unit costs related to the compared interventions were presented to the GDG to inform the possible economic implication of the recommendation to make.

Number of Source Documents

The number of studies identified for each clinical question is provided in Appendix D in the full version of the original guideline document (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Evidence of Effectiveness

The research fellows:

- Critically appraised relevant studies using the appropriate checklist as specified in the Guidelines Manual (2009) (available from: www.nice.org.uk [see also the "Availability of Companion Documents" field]).
- Extracted key information about the study's methods and results, and transferred it into evidence tables (evidence tables are included in Appendix G of the full version of the original guideline document).
- Generated summaries of the evidence by outcome (included in the relevant chapter write-ups):
    - Randomised studies: meta analysed where appropriate, and reported in Grading of Recommendations Assessment, Development and Evaluation (GRADE) profiles
    - Observational studies: data presented as a range of values in GRADE profiles
    - Diagnostic studies: data presented as a range of values in adapted GRADE profiles
    - Prognostic studies: data from each study were summarised in a table and/or presented in a narrative
    - Qualitative studies: each study was summarised in a table where possible, but otherwise presented in a narrative

Twenty per cent (20%) of each of the above stages of the reviewing process was quality assured by the second reviewer to eliminate any potential of reviewer bias or error.

Methods of Combining Clinical Studies

Data Synthesis for Intervention Reviews

Where possible, meta-analyses were conducted to combine the results of studies for each outcome in each review question. Cochrane Review Manager (RevMan5) software was used for this purpose.

Binary Outcomes

Fixed-effects (Mantel-Haenszel) techniques, using an inverse variance method for pooling, were used to calculate risk ratios (relative risk) for the binary outcomes which were:

- The existence of patient-assessed symptoms
- Patient satisfaction
- Reflux or clinical recurrence
- Adverse events
- Development of complications of varicose veins

In addition to relative effects, absolute effect sizes were also calculated using the GRADEpro software, using the median event rate across the control arms of the individual studies in the meta analysis.

For variables where there were zero events in the comparator arm, Peto odds ratios, rather than risk ratios were calculated. Peto odds ratios are more appropriate for data with a low number of events.

Continuous Outcomes

The continuous outcomes were analysed using an inverse variance method for pooling weighted mean differences. These outcomes were:

- Quality of life
- Physician reported disease measures
- Symptom scales (normally visual analogue scale [VAS])
- Days to return to work/normal activity

Where the studies within a single meta-analysis had different continuous scales, standardised mean differences were used. This involved each study's mean difference measure being 'normalised' to the pooled intervention and comparator group standard deviation value. For example, if the

mean difference was 18 and the pooled standard deviation value was 9, then the standardised mean difference would be 18/9 = 2.

The means and standard deviations of continuous outcomes were required for meta-analysis. In cases where standard deviations were not reported, the standard error of the mean difference was calculated from the mean difference values and either p-values or confidence intervals. Meta-analysis was then undertaken using the generic inverse variance method in Cochrane Review Manager (RevMan5.1) software. Where p values were reported as 'less than,' a conservative approach was undertaken. For example, if p value was reported as 'p ≤0.001', the calculations for standard error were based on a p value of 0.001. If p values or confidence intervals were not available then the methods described in Section 16.1.3 of the Cochrane Handbook (version 5.1.0, updated March 2011) were applied if possible. If these were not possible to apply, then meta-analysis was not carried out.

Statistical heterogeneity was assessed for both binary and continuous outcomes by visually examining the forest plots, and by considering the chi-squared test for significance at p <0.1 and the I-squared inconsistency statistic (with an I-squared value of more than 50% indicating considerable heterogeneity). Where considerable heterogeneity was present, sensitivity analyses was carried out. Sensitivity analyses were carried out looking at the subgroups which were pre-specified by the Guideline Development Group (GDG). If the heterogeneity still remained, a random effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect. For further details on assessing inconsistency see Section 3.3.4.2 of the full version of the original guideline document.

Data Synthesis for Prognostic Factor Reviews

Odds ratio, relative risks, or hazard ratios, with their 95% confidence intervals, from multivariate analyses were extracted from the papers. Because of the nature of the evidence collected, with high variability of risk factors, outcomes and confounders considered, no quantitative data synthesis was carried out. Evidence was synthesised in narrative form.

Data Synthesis for Diagnostic Test Accuracy Review

For diagnostic test accuracy studies, no meta-analysis of evidence was varied out. The following outcomes were reported for each test: sensitivity, specificity, positive predictive value, and negative predictive value. In cases where the outcomes were not reported, 2 by 2 tables were constructed from raw data to allow calculation of these accuracy measures. Summary receiver operative characteristic (ROC) curves were not generated as there were insufficient studies (<5) per test to allow a curve to be produced.

Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included randomised controlled trials (RCT) and observational studies were evaluated and presented using an adaptation of the 'GRADE toolbox' developed by the international GRADE working group (http://www.gradeworkinggroup.org/). The software (GRADEpro) developed by the GRADE working group was used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results. The 'summary of findings' were presented in a single GRADE table in this guideline. The 'Clinical/Economic Study Characteristics' section of the table includes details of the quality assessment while the 'Clinical/Economic Summary of Findings' section table includes pooled outcome data (where appropriate), an absolute measure of intervention effect, and the summary of quality of evidence for that outcome.

The evidence for each outcome was examined separately for the quality elements listed and defined in Table 2 in the full version of the original guideline document and each graded using the quality levels listed in the "Rating Scheme for the Strength of the Evidence" field. The main criteria considered in the rating of these elements are discussed below. The ratings for each component were summed to obtain an overall assessment for each outcome.

Grading the Quality of Clinical Evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

1. A quality rating was assigned, based on the study design. RCTs start HIGH and observational studies as LOW, uncontrolled case series as LOW.
2. The rating was then downgraded for the specified criteria: Risk of bias (study limitations), inconsistency, indirectness, imprecision, and publication bias. Evidence from observational studies (that had not previously been downgraded) was upgraded if there was: a large magnitude of effect, dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have a "serious" or "very serious" risk of bias was rated at 1 or 2 points respectively.
3. The downgraded/upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as HIGH and the overall quality became MODERATE, LOW, or VERY LOW if 1, 2, or 3 points were deducted respectively.

4. The reasons used for downgrading were specified in the footnotes.

The details of criteria used for each of the main quality elements are discussed further in Sections 3.3.4.1 to 3.3.4.5 in the full version of the original guideline document.

Appraising the Quality of Evidence for Prognostic Studies

The evidence for prognostic studies was evaluated according to the criteria given in Table 5 in the full version of the original guideline document (study design, patient recruitment, validity of risk factor measure[s], validity of outcome measure, blinding, adequate follow-up [or retrospective] duration, confounder consideration, attrition, directness).

Because prognostic reviews were not usually based on multiple outcomes per study, quality rating was assigned by study. However if there was more than one outcome involved in a study, then the quality rating of the evidence statements for each outcome was adjusted accordingly. For example, if one outcome was based on an invalidated measurement method, but another outcome in the same study wasn't, the latter outcome would be graded one grade higher than the other.

Quality rating started at HIGH for prospective studies, and each major limitation (see "Appraising the Quality of Evidence by Outcomes," above) brought the rating down by one level to a minimum grade of LOW, as explained for interventional studies.

Appraising the Quality of Evidence for Diagnostic Studies

Evidence for diagnostic data was evaluated by study, using the Quality Assessment of Diagnostic Accuracy Studies version 2 (QUADAS-2) checklists. Risk of bias and applicability in primary diagnostic accuracy studies in QUADAS-2 consists of 4 domains (see Table 6 in the full version of the original guideline document):

- Patient selection
- Index test
- Reference standard
- Flow and timing

Clinical Evidence Statements

Clinical evidence statements are summary statements that are presented after the GRADE profiles, summarising the key features of the clinical effectiveness evidence presented. The wording of the evidence statements reflects the certainty/uncertainty in the estimate of effect. The evidence statements are presented by outcome and encompass the following key features of the evidence:

- The number of studies and the number of participants for a particular outcome
- An indication of the direction of clinical importance (if one treatment is beneficial or harmful compared to the other, or whether there is no difference between the two tested treatments)
- A description of the overall quality of evidence (GRADE overall quality)

Qualitative Methodology

Qualitative data provides information of people's thoughts, feelings, attitudes, and beliefs. As such data is necessarily subjective, there is no requirement for it to be representative of the wider population; instead it is framed in the unique context of the individual respondent. Nevertheless, these data need to be trustworthy in terms of accurately reflecting the actual opinions of the respondent. To this end qualitative literature was evaluated in terms of whether there had been adequate triangulation of methods and researchers, member checking, and methodological transparency. Qualitative methods started at HIGH, and each limitation reduced the grading by one increment, through MODERATE and LOW to VERY LOW.

Qualitative review findings from different studies were pooled and categorised in a manner that emerged from the findings.

Evidence of Cost-effectiveness

Literature Review

The health economist:

- Critically appraised relevant studies using the economic evaluations checklist as specified in the Guidelines Manual (see the "Availability of Companion Documents" field)
- Extracted key information about the study's methods and results into evidence tables (evidence tables are included in Appendix H in the full

version of the original guideline document)
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter write-ups in the full version of the original guideline document)

NICE Economic Evidence Profiles

The NICE economic evidence profile has been used to summarise cost and cost-effectiveness estimates. The economic evidence profile shows, for each economic study, an assessment of applicability and methodological quality, with footnotes indicating the reasons for the assessment. These assessments were made by the health economist using the economic evaluation checklist from The Guidelines Manual. It also shows incremental costs, incremental outcomes (for example, QALYs) and the incremental cost-effectiveness ratio from the primary analysis, as well as information about the assessment of uncertainty in the analysis. See Table 7 in the full version of the original guideline document for more details.

If a non-UK study was included in the profile, the results were converted into pounds sterling using the appropriate purchasing power parity.

Where economic studies compare multiple strategies, results are presented in the economic evidence profiles for the pair-wise comparison specified in the review question, irrespective of whether or not that comparison was 'appropriate' within the analysis being reviewed. A comparison is 'appropriate' where an intervention is compared with the next most expensive non-dominated option – a clinical strategy is said to 'dominate' the alternatives when it is both more effective and less costly. Footnotes indicate if a comparison was 'inappropriate' in the analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

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This guidance was developed in accordance with the methods outlined in the NICE Guidelines Manual 2009 (see the "Availability of Companion Documents" field).

A multidisciplinary Guideline Development Group (GDG) comprising professional group members and consumer representatives of the main stakeholders developed this guideline. The group met every 4 to 6 weeks during the development of the guideline.

Developing Recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendices G and H in the full version of the original guideline document
- Summary of clinical and economic evidence and quality (as presented in Chapters 5 to 11 in the full version of the original guideline document)
- Forest plots (see Appendix I in the full version of the original guideline document)
- A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (see Appendix L in the full version of the original guideline document)

Recommendations were drafted on the basis of the GDG interpretation of the available evidence, taking into account the balance of benefits, harms, and costs. When clinical and economic evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on their expert opinion. The considerations for making consensus based recommendations include the balance between potential harms and benefits, economic costs or implications compared to the benefits, current practices, recommendations made in other relevant guidelines, patient preferences, and equality issues. The consensus recommendations were done through discussions in the GDG. The GDG also considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation. The wording of recommendations was agreed by the GDG and focused on the following factors:

- On the actions health professionals need to take
- Include what readers need to know

- Reflect the strength of the recommendation (for example the word 'offer' was used for strong recommendations and 'consider' for weak recommendations)
- Emphasise the involvement of the patient (and/or their carers if needed) in decisions on treatment and care
- Follow NICE's standard advice on recommendations about drugs, waiting times, and ineffective interventions

The main considerations specific to each recommendation are outlined in the "Evidence to Recommendation" section for each chapter of the full version of the original guideline document.

Groups for Special Consideration

Pregnant Women with Varicose Veins

The evidence for this population group was summarised to inform specific and easily accessible recommendations. The information is presented in Chapter 11 in the full version of the original guideline document.

People with Recurrent Varicose Veins

The evidence for this population was discussed by the GDG but it was felt that separate recommendations were not required. Where the recommendation is relevant to people with recurrent varicose veins this has been made explicit in the wording of the recommendation.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

Undertaking New Health Economic Analysis

As well as reviewing the published economic literature for each review question, as described above, new economic analysis was undertaken by the Health Economist in a priority area. The priority area for new health economic analysis was agreed by the Guideline Development Group (GDG) after formation of the review questions and consideration of the available health economic evidence.

To parameterise treatment effects in the model, a network meta-analysis (NMA) was carried out. This type of analysis simultaneously compares multiple treatments in a single meta-analysis, preserving the randomisation of randomised controlled trials (RCTs) included in the reviews of direct comparisons. The aim of the NMA was to include all relevant evidence in order to calculate treatment-specific hazard ratios for use in the model. We used statistical models for fixed and random effects that allowed inclusion of multi arm trials and accounted for the correlation between arms in

the trials with any number of trial arms. The code for the NMA was adapted from the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) website, and run in WinBUGS 14. Heterogeneity and inconsistency were investigated using the methods described in Dias et al (2012)28 and Dias et al (2012a).29 Further details about the NMA can be found in Appendix L and the NMA code in Appendix M in the full version of the original guideline document (see the "Availability of Companion Documents" field).

Additional data for the analysis was identified as required through additional literature searches undertaken by the health economist, and discussion with the GDG. Model structure, inputs and assumptions were explained to and agreed by the GDG members during meetings, and they commented on subsequent revisions.

Cost-effectiveness Criteria

In general, an intervention was considered to be cost-effective if either of the following criteria applied (given that the estimate was considered plausible):

a. The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
b. The intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'from evidence to recommendations' section of the relevant chapter with reference to issues regarding the plausibility of the estimate or to the factors set out in the NICE report 'Social value judgements: principles for the development of NICE guidance'.

If a study reported the cost per life year gained but not QALYs, the cost per QALY gained was estimated by multiplying by an appropriate utility estimate to aid interpretation. The estimated cost per QALY gained is reported in the economic evidence profile with a footnote detailing the life-years gained and the utility value used. When QALYs or life years gained are not used in the analysis, results are difficult to interpret unless one strategy dominates the others with respect to every relevant health outcome and cost.

See Appendix L in the full version of the original guideline document for details of the health economic analysis undertaken for the guideline.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guidance is subject to a 6 week public consultation and feedback as part of the quality assurance and peer review the document. All comments received from registered stakeholders are responded to in turn and posted on the National Institute for Health and Care Excellence (NICE) Web site when the pre-publication check of the full guideline occurs.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of varicose veins in the legs

See the "Tradeâ€off between clinical benefits and harms" sections in the full version of the original guideline document (see the "Availability of Companion Documents" field) for additional details about benefits of specific interventions.

Potential Harms

- Being female was associated with an increased risk of complications after foam sclerotherapy compared with being male.
- There was a higher rate of nerve injury in people undergoing stripping surgery compared to foam sclerotherapy with crossectomy.
- Post-operative pain was greater at 10 to 14 days for stripping surgery compared to radiofrequency ablation, but also greater at 10 to 14 days for laser surgery compared to stripping surgery.
- The Guideline Development Group (GDG) noted that from a patient perspective negative experiences with use of compression, such as the difficulty in putting on stockings, could result in non-adherence.
- Adverse events related to compression stockings were not reported in the included studies and were considered minimal by the GDG.
- There appeared to be an important disadvantage of surgery with compression in terms of a slower return to work compared with surgery alone.
- The potential benefits of compression after interventional treatment need to be balanced against the potential costs of compression and any harm (such as comfort for the patient).

See the "Trade off between clinical benefits and harms" and "Adverse events" sections in the full version of the original guideline document (see the "Availability of Companion Documents" field) for additional details about harms of specific interventions.

Contraindications

Contraindications

The Guideline Development Group noted huge anatomical variations in the superficial venous system, especially in the region of the popliteal fossa, bifid great saphenous veins, and extra-fascial location of the great saphenous veins, which might contraindicate endovenous thermal ablation.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If someone does not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent , the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.
- The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual

patients.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) has developed tools to help organisations implement this guidance. These are available on the NICE Web site (see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Referral to a Vascular Service

- Refer people to a vascular service[1] if they have any of the following.
  - Symptomatic[2] primary or symptomatic recurrent varicose veins
  - Lower-limb skin changes, such as pigmentation or eczema, thought to be caused by chronic venous insufficiency
  - Superficial vein thrombosis (characterised by the appearance of hard, painful veins) and suspected venous incompetence
  - A venous leg ulcer (a break in the skin below the knee that has not healed within 2 weeks)
  - A healed venous leg ulcer

Assessment and Treatment in a Vascular Service

Assessment

- Use duplex ultrasound to confirm the diagnosis of varicose veins and the extent of truncal reflux, and to plan treatment for people with suspected primary or recurrent varicose veins.

Interventional Treatment

- For people with confirmed varicose veins and truncal reflux:
  - Offer endothermal ablation (see the NICE guidelines Radiofrequency ablation of varicose veins [NICE interventional procedure guidance 8] and Endovenous laser treatment of the long saphenous vein [NICE interventional procedure guidance 52).
  - If endothermal ablation is unsuitable, offer ultrasound-guided foam sclerotherapy (see the NICE guideline Ultrasound-guided foam sclerotherapy for varicose veins [NICE interventional procedure guidance 440]).
  - If ultrasound-guided foam sclerotherapy is unsuitable, offer surgery.
    If incompetent varicose tributaries are to be treated, consider treating them at the same time.

Non-interventional Treatment

- Do not offer compression hosiery to treat varicose veins unless interventional treatment is unsuitable.

[1]A team of healthcare professionals who have the skills to undertake a full clinical and duplex ultrasound assessment and provide a full range of treatment.

[2]Veins found in association with troublesome lower limb symptoms (typically pain, aching, discomfort, swelling, heaviness, and itching).

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Clinical Guideline Centre. Varicose veins in the legs. The diagnosis and management of varicose veins. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. 23 p. (Clinical guideline; no. 168).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Jul

Guideline Developer(s)

National Clinical Guideline Centre - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members declared interests including consultancies, fee-paid work, share-holdings, fellowships, and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest, which were also recorded (see Appendix B in the full version of the original guideline document [see the "Availability of Companion Documents" field]).

Members were either required to withdraw completely, or for part of the discussion, if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B in the full version of the original guideline document.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Varicose veins in the legs. The diagnosis and management of varicose veins. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. 250 p. (Clinical guideline; no 168). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Care Excellence (NICE) Web site .
- Varicose veins in the legs. The diagnosis and management of varicose veins. Appendices. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. 401 p. (Clinical guideline; no 168). Electronic copies: Available in PDF from the NICE Web site .
- Varicose veins in the legs. The diagnosis and management of varicose veins. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. (Clinical guideline; no 168). Electronic copies: Available from the NICE Web site .
- Varicose veins in the legs. The diagnosis and management of varicose veins. Clinical audit tool. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. (Clinical guideline; no 168). Electronic copies: Available from the NICE Web site .
- Varicose veins in the legs. The diagnosis and management of varicose veins. Costing report. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. 23p. (Clinical guideline; no 168). Electronic copies: Available in PDF from the NICE Web site

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- Varicose veins in the legs. The diagnosis and management of varicose veins. Costing template. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. (Clinical guideline; no 168). Electronic copies: Available from the NICE Web site .
- Varicose veins in the legs. NICE pathway. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. Electronic copies: Available from the NICE Web site .
- The guidelines manual 2009. London (UK): National Institute for Health and Care Excellence (NICE); 2009 Jan. Electronic copies: Available in PDF from the NICE Archive Web site .

Patient Resources

The following is available:

- Varicose veins in the legs. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Jul. Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download as a Kindle or EPUB ebook from the NICE Web site . Also available in Welsh from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI on November 15, 2013.

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